CKD-MBD Post Kidney Transplantation

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NHS Foundation Trust

Overview of the talk

- Challenges in diagnosis of CKD-MBD post transplantation
- Prevalence of CKD-MBD post transplantation
- Cardiovascular risk in CKD-MBD post transplantation
- Monitoring of CKD-MBD post transplantation
- Management of CKD-MBD post transplantation

Introduction CKD-MBD Post Transplantation

- Most of the biochemical abnormalities associated with CKD-MBD correct post transplantation. However the complete normalization of biochemical abnormalities is not assured
- Failure of normalisation of PTH post kidney transplant may predispose the patient to fractures, muscular, bone and joint pains
- CKD-MBD is also associated with cardiovascular risk in this population and not adequately managed

Challenges in CKD-MBD Post Transplantation

- The etiology of CKD-MBD post transplantation is multifactorial
- Pre-existing CKD–MBD from CKD 5
- Low BMD or loss of BMD does not predicts fracture
- No RCT examining bone-specific therapies on patient-level outcomes, mortality or fractures
- Bone biopsy studies are limited post transplantation

Challenges in CKD-MBD Post Transplantation Transplant specific

- Rapidly changing GFR T
- The degree of kidney function recovery
- The effects of immunosuppressive and other therapies
- Heterogeneous patient population

What happens to CKD-MBD Post Transplant?

- Hypophosphatemia occurs immediately after tx, but once kidney function has become stabilized, serum phosphorus returns to the normal range
- Serum calcium tends to increase after transplant and then stabilizes at the higher end of the normal range within few months
- PTH levels decrease significantly during the first 3 months after transplant but typically stabilize at elevated values after 1 year
- Low levels of 1,25(OH)2D typically do not reach normal values until almost 18 months after transplant

No large databases in which these data are routinely collected
Most reports from single-center studies

Fibroblast growth factor-23 FGF-23 post transplant

- Recent research showed persistent post transplant elevations of fibroblast growth factor-23 (FGF-23) as playing a major role in post transplant hypophosphatemia and suppression of 1α-hydroxylase activity in the kidney
- There is limited information regarding FGF-23 relationship to mineral metabolism in prevalent kidney transplant recipients

Audit of CKD-MBD Post Renal Transplantation

Murtaza A, Ali H, Bali T, Ahmed A
Renal Department, Royal Preston Hospital, Lancashire Teaching Hospitals NHS

Biochemical Parameters ± Standard Error	Pre-Transplant (1 month before transplantation)	Months After Renal Transplantation				
		0 (at transplantation)	3	6	9	12
Corrected Calcium (mmol/L) P-value	2.34 ± 0.02	2.23 ± 0.04 P = 0.173	2.48 ± 0.03 P = 0.0007	2.48 ± 0.02	2.52 ± 0.02	2.49 ± 0.02
PTH (pmol/L) P-value	47.21 ± 5.17	53.17 ± 14.94 P =0.7142	34.70 ± 9.08 P = 0.0415	18.33 ± 3.56 P < 0.0001	18.29 ± 3.87	20.28 ± 4.29
ALP(u/L) P-value	116.55 ± 10.61	100.45 ± 16.51 P = 0.0509	127.75 ± 11.76 P = 0.6397	141.96 ± 11.60 P = 0.0136	129.97 ± 10.60 P = 0.0464	123.85 ± 8.89 P = 0.0671
Phosphate (mmol/L) P-value	1.66 ± 0.05	1.29 ± 0.10 P < 0.0001	0.93 ± 0.06	0.96 ± 0.05	0.93 ± 0.03	0.97 ± 0.04

Audit of CKD-MBD Post Renal Transplantation

Murtaza A, Ali H, Bali T, Ahmed A

Renal Department, Royal Preston Hospital, Lancashire Teaching Hospitals NHS

Medication	Main Ingredient(s)	Prior to Transplantation		Months Following Transplant					
				0		6		12	
		No. of patients & percentage	Mean dose ± SE	No. of patients & percentage	Mean dose ± SE	No. of patients & percentage	Mean dose ± SE	No. of patients & percentage	Mean dose ± SE
Alfacalcidol (weekly dose, mcg)	1-hydroxycholecalciferol	46 56.1 %	2.41 ± 0.17	5 5.8 %	3.63 ± 0.72	17.1 19.8 %	2.90 ± 0.45	17 20%	3.44 ± 0.57
Adcal D3 (g/day)	Calcium carbonate	1 1.03 %	9.00	0	0	1.2 1.03 %	1.5	4 4.7 %	1.875 ± 0.375
Calcichew (g/day)	Calcium carbonate	4 4.7 %	3.32 ± 0.31	3.5	3.67 ± 0.33	4 4.7 %	3.40 ± 0.40	3 3.5 %	2.67 ± 0.67
Phosex (mg/day)	Calcium acetate	15 17.4 %	2933.3 ± 266.6	0	0	0	0	0	0
Phoslo (mg/day)	Calcium acetate	11 12.8	2970.6 ± 398.2	0	0	0	0	0	0
Lanthanum (mg/day)	Lanthanum carbonate	16 18.6 %	2359.4 ± 239.3	0	0	0	0	0	0
Renagel (mg/day)	Sevelamir hydrochloride	8 9.3 %	4088.9 ± 488.89	0	0	0	0	0	0
Renvela (mg/day)	Sevelamir carbonate	3 3.5 %	5066.7 ± 1162.4	0	0	0	0	0	0
Cinacalcet (mg/day)		7 8.1 %	64.3 ± 7.8	1 1.2	60.0	4 4.7 %	45.00 ± 8.66	6 7 %	50.0 ± 6.32

Risk factors for CKD-MBD Post Transplant

- MBD-CKD pre transplant
    - Low and high PTH pre transplant
- Impaired graft function
- pre-existing osteomalacia
- Medications-glucocorticoid exposure
- Younger age at transplantation
- Vitamin D deficiency
- High Serum FGF 23
- post- menopausal status and hypogonadism
- Diabetes, smoking, physical activity, and
- Duration of dialysis and transplantation

Immunosuppressive Medications

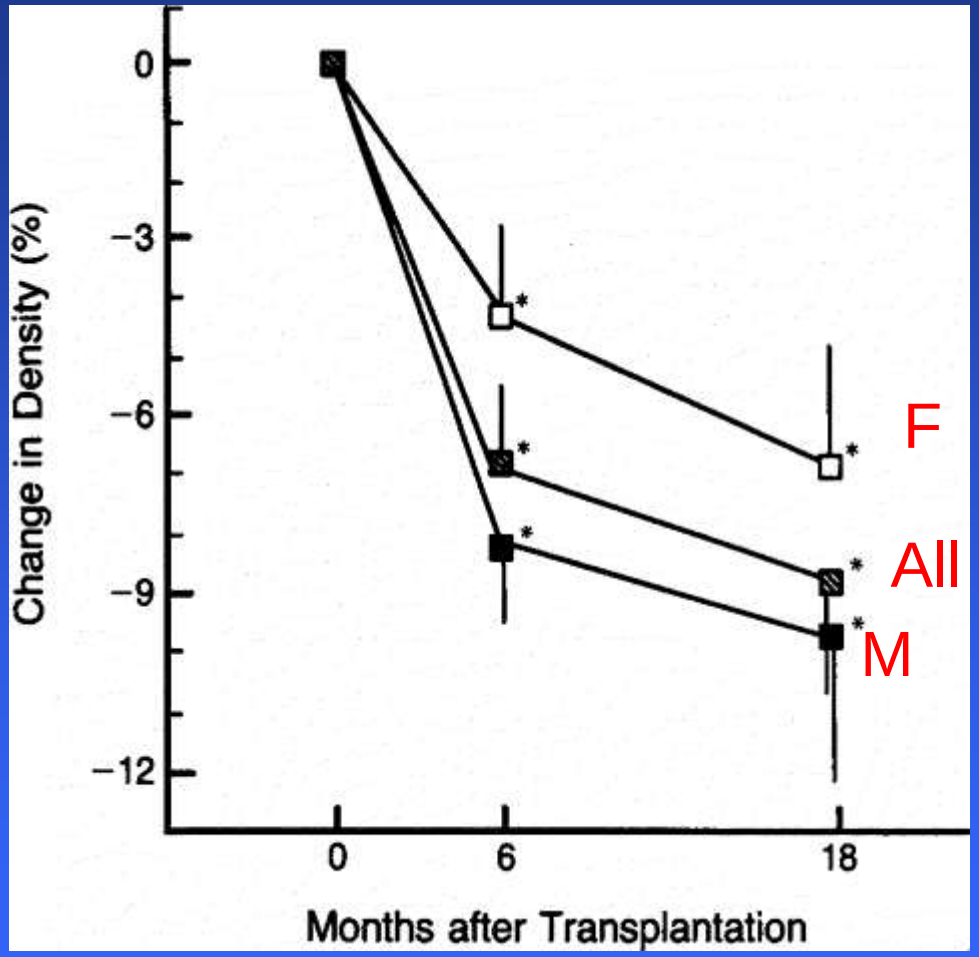
Glucocorticoids- Clear evidence – Bone Loss

CNI; Cyclosporine and Tacrolimus-No clear effect

mTOR Inhibitors- No Clear Effect

Azathiopurine/Mycophenolic Acid- No Effect

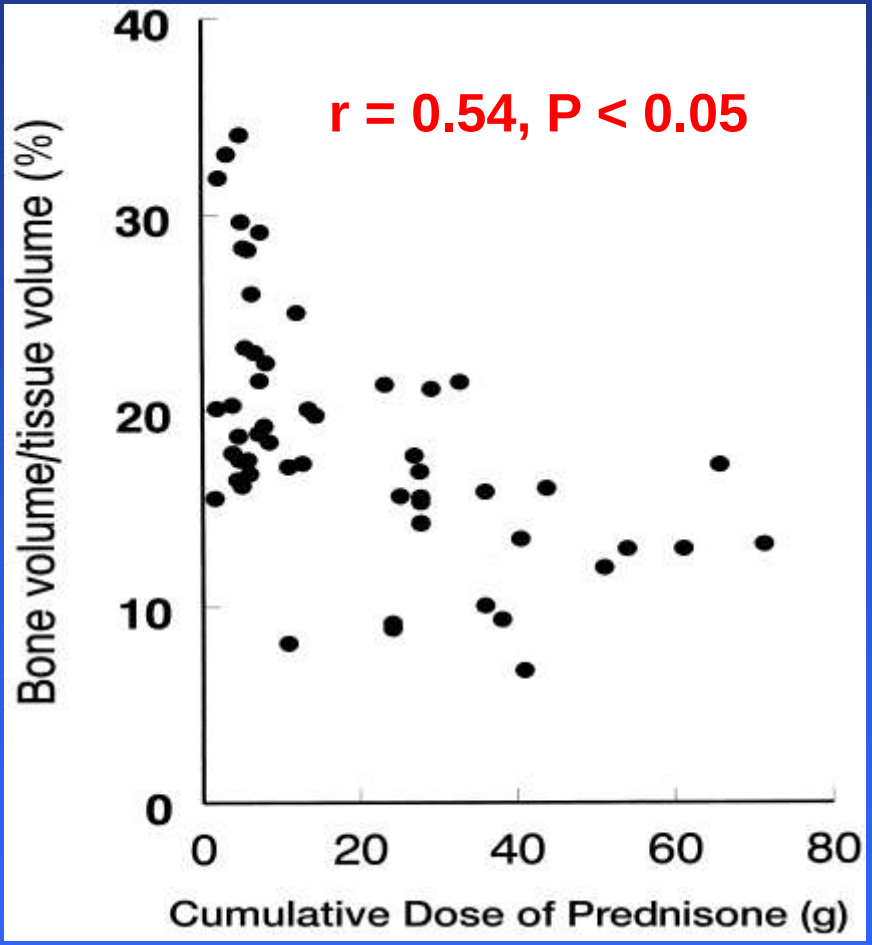
Bone Loss Post Transplant
Percent Changes in BMD of the Lumbar Vertebrae



- Small Study US, 20 patients follow up to 18 months
- Osteopenia associated with renal transplantation due to glucocorticoids
- As a consequence, fractures are common and associated with substantial morbidity

Julian BA et al. N Engl J Med 1991;325:544-550.

Relationship between cumulative dose of prednisone and bone loss post kidney transplant



- Kentucky, USA. 57 adult post transplants had bone biopsies (32 men and 25 women), Tx 5.6 yr before biopsy
- **Bone turnover :**
- low in 45.6%, normal in 28.1%, and high in 26.3%
- Mineralization was prolonged in 87.5% (21 patients with osteomalacia and focal osteomalacia
- Normal serum levels of calcidiol and calcitriol suggests vitamin D resistance

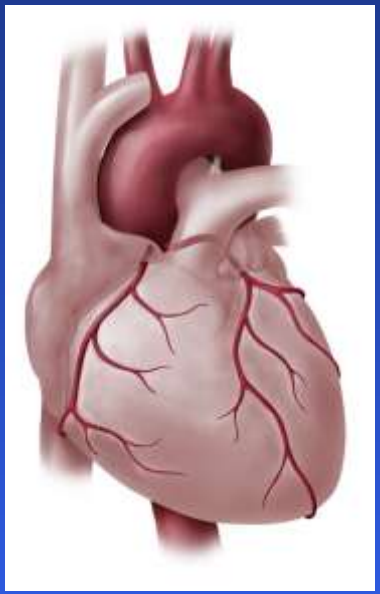
MARIE-CLAUDE MONIER-FAUGERE et al. JASN 2000;11:1093-1099

Cardiovascular risk and calcification post Kidney transplant

Risk factors for Cardiovascular Disease in CKD5

Traditional

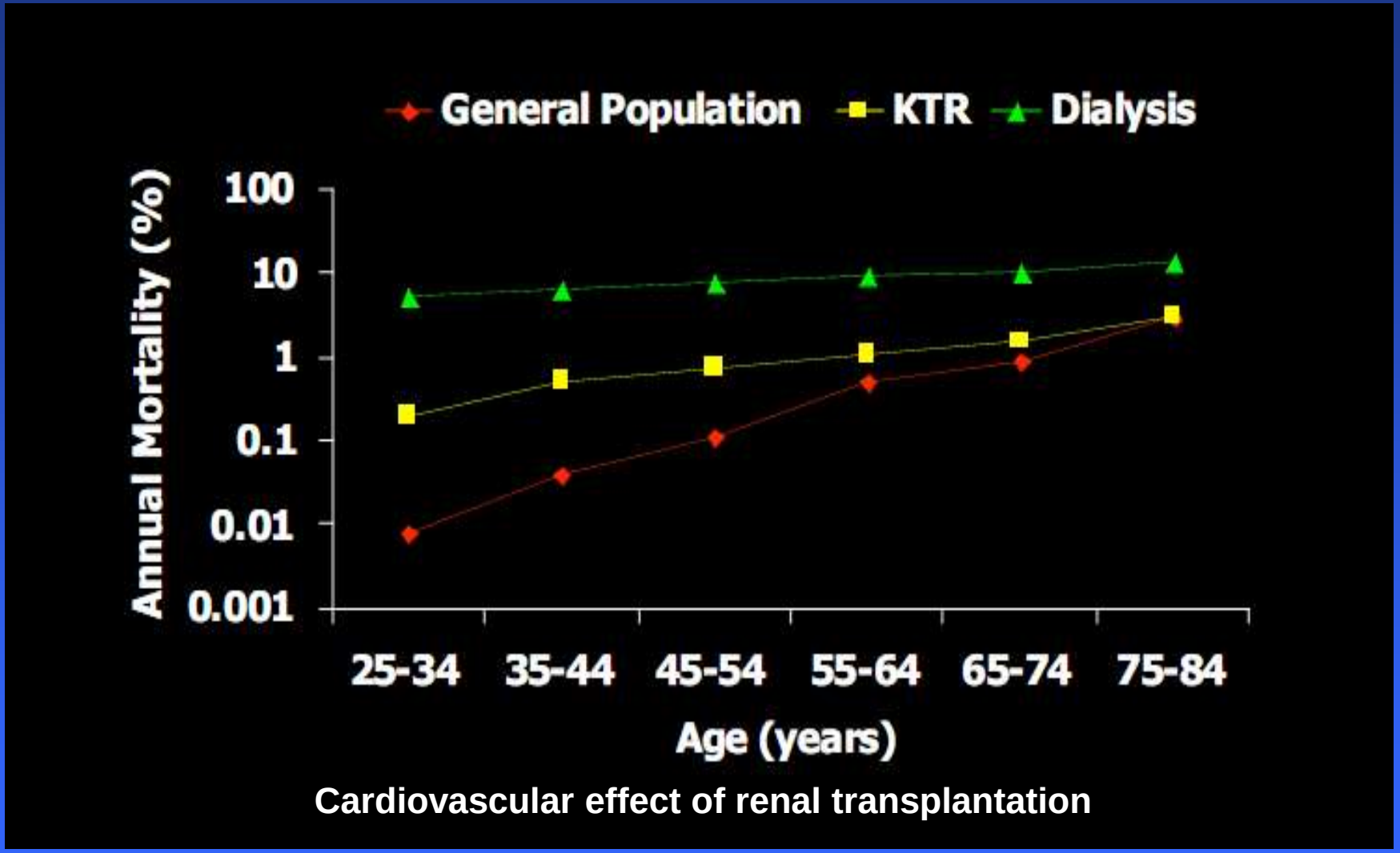
- Hypertension….. LVH
- Diabetes
- Smoking
- Hyperlipidaemia



Non traditional

- Anemia
- Secondary hyperparathyroidism……..CKD-MBD
- Hyperhomocysteineamia
- Oxidant stress and inflammation …high CRP

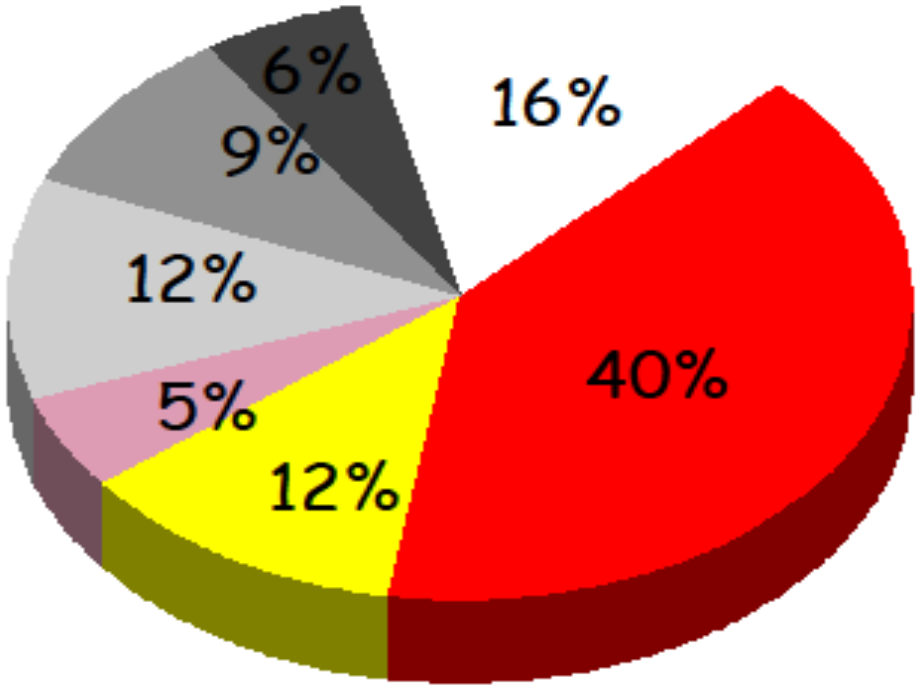
Survival



Cardiovascular effect of renal transplantation

Foley, Am J Kidney Dis, 1998;32(S1):8

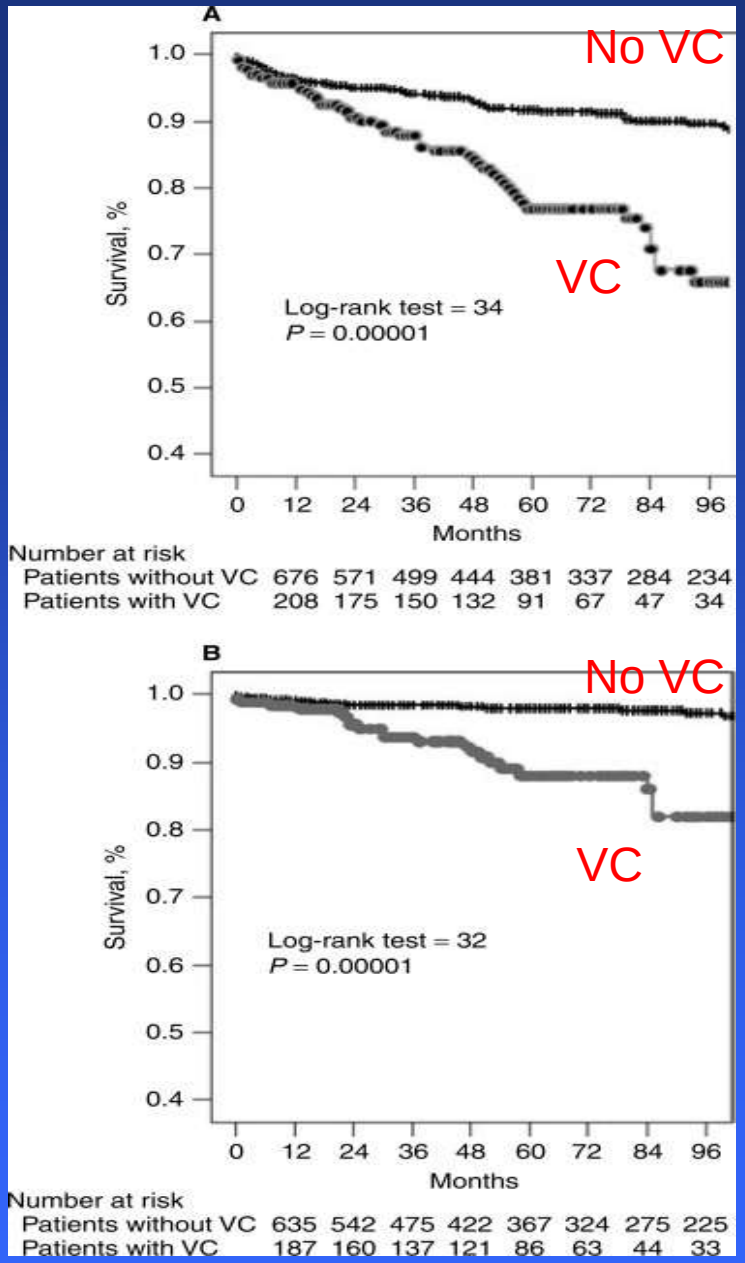
Cause of death in renal transplant recipients



- Cardiac
- Stroke
- Vascular disease
- Malignancy
- Infection
- Other
- Unknown

1st grafts 1984-1996
92 deaths in 1260 patients

Source:Kavanagh et al, Nephron 1999;81:109

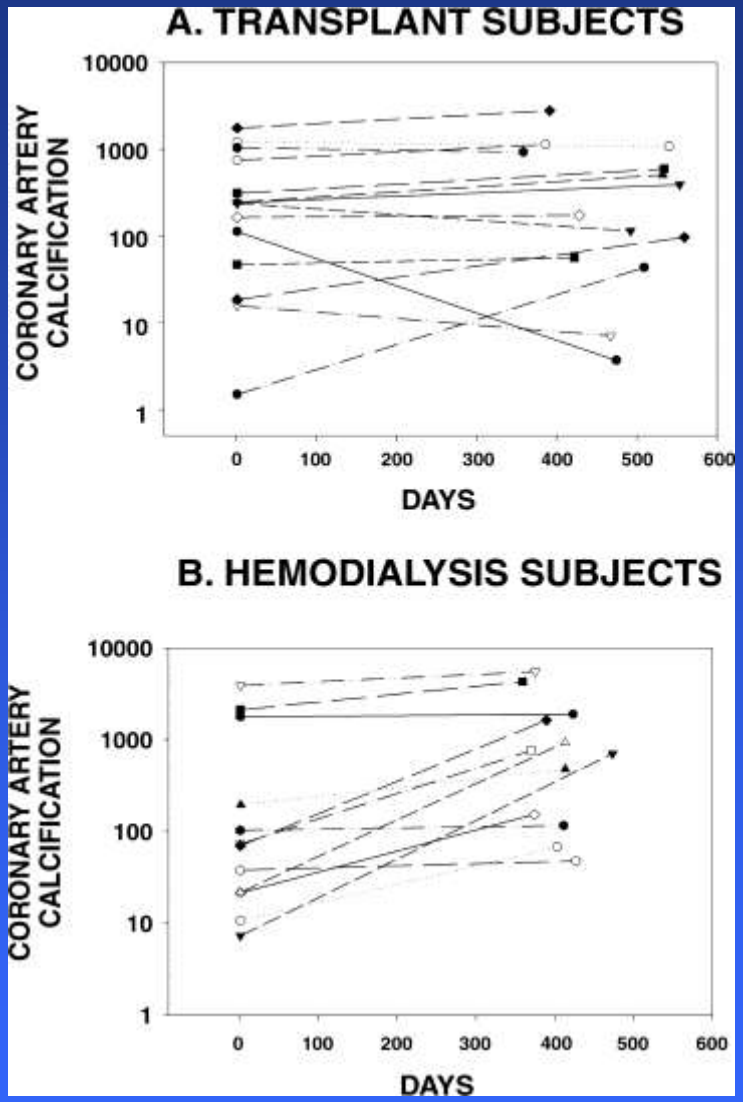


Kidney International 2005 67, 2015-2020DOI

Vascular calcification post Kidney Tx

- Spanish Study 1117 RT recipients investigated the association between long-term survival and the presence of VC, preoperative posteroanterior plain radiography from aorto-iliac region, at the time of Tx. The primary study outcome was all-cause mortality
- VC were observed in 273 patients (24.4%) before RT, 132 (12%) patients died during follow-up, mainly, to cardiovascular cause
- Plain abdominal X-ray is less sensitive than CT and gives only semi- quantitative information. The main limitation in interpreting calcification in the transplant population is the carryover effect from CKD stage 5 or stage 5D

Change in coronary artery calcification over time

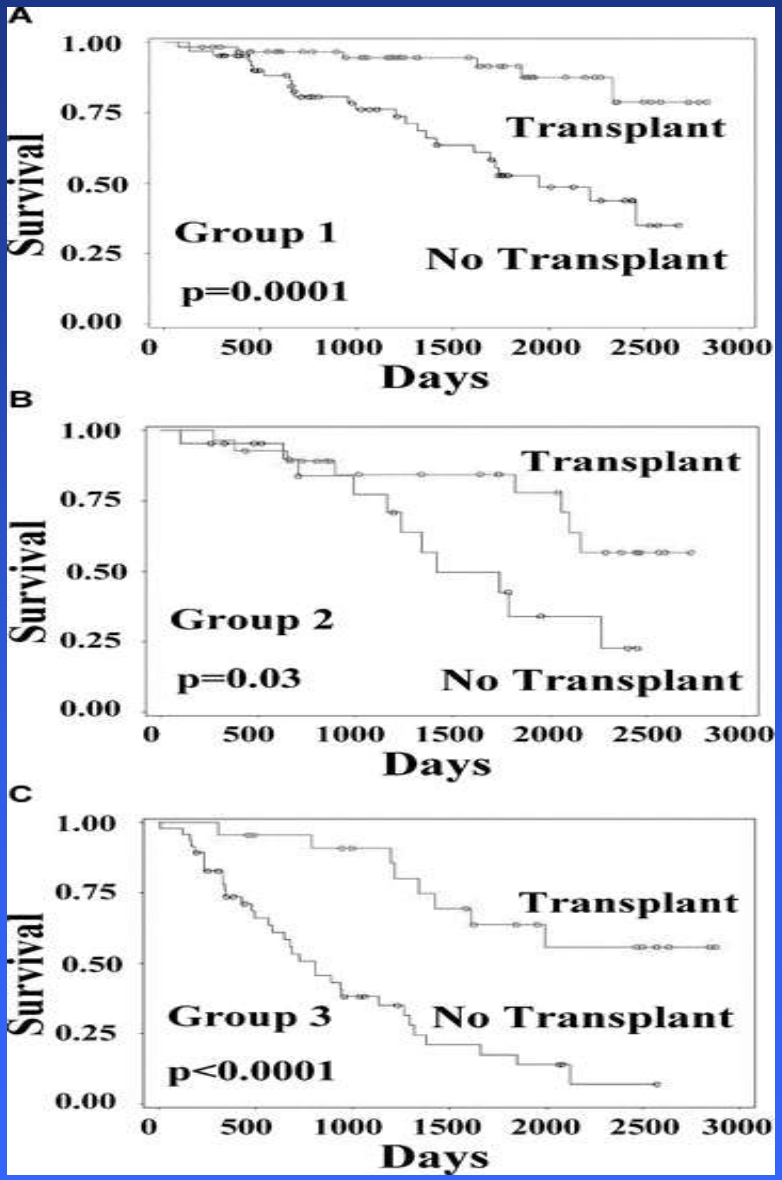


Sharon M. Moe et al. Nephrol. Dial. Transplant. 2004;19:2387-2393

American Study
Two cohorts were evaluated for the natural history of vascular calcification:

- A: 23 patients who underwent a baseline CT scan at the time of renal transplant and a repeat evaluation 15-20 months later; and
- B: 33 chronic kidney disease, stage 5 haemodialysis subjects who underwent a baseline CT scan, all followed for a minimum of 15 months, and 17 of whom underwent a second CT scan
- Renal transplantation appears to slow down or arrest CAC, whereas CAC progresses in haemodialysis patients

Extent and Severity of Coronary Disease and Mortality in Patients with ESRD valuated for Renal Transplantation



Jones et al, 2009 AJT, 9,8. 1846-1852

Monitoring CKD-MBD Post Transplant KDIGO 2009

- In patients in the immediate post-kidney transplant period-weekly until stable
- In CKD stages 1–3T -every 6–12 months; and for PTH, once, with subsequent intervals depending on baseline level and CKD progression
- In CKD stage 4T-every 3–6 months; and for PTH, every 6–12 months
- In CKD stage 5T-every 1–3 months; and for PTH, every 3–6 months
- In CKD stages 3–5T, measurement of alkaline phosphatases annually, or more frequently in the presence of elevated PTH

Management of CKD-MBD Post Transplant

- Vitamin D +/- Calcium supplements
- Steroid withdrawal
- Calcitriol
- Calcitonin
- Bisphosphonates
- Calcimimetics
- Parathyroidectomy

Management of CKD-MBD Post Transplant 2

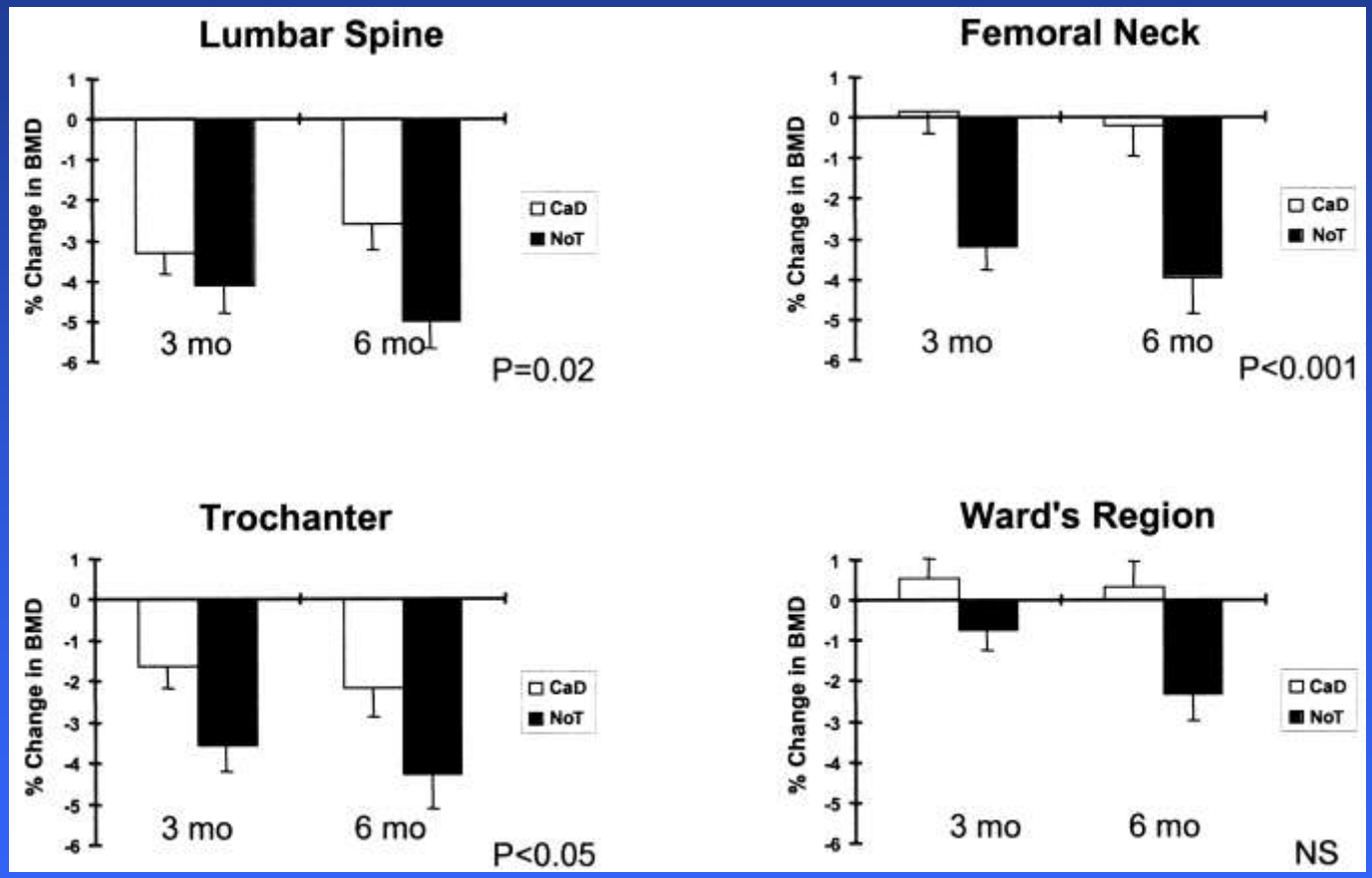
- Limited number of post-transplant studies utilizing these drugs have not yet documented improved fracture prevention, hospitalisation or fracture-related mortality and have not considered allocation based on risk factors for fracture or markers of bone turnover

- DXA should be reserved for high-risk populations, including those receiving significant doses of corticosteroids, or those with risk factors for osteoporosis, also in a well- functioning allograft (CKD stages 1–3T), as patients with CKD stages 4–5T will be more likely to have abnormal bone quality from CKD–MBD, with unknown impact on the predictive value of DXA

Nutritional 25(OH)D

- 25(OH)D deficiency and insufficiency post kidney transplant should be corrected using treatment strategies recommended for the general population
- no RCTs of vitamin D supplementation in patients with a kidney transplant evaluating end points other than bone health
- Vitamin D deficiency and insufficiency are associated with cardiovascular disease, autoimmune disorders, malignancies, bone disease and musculoskeletal weakness, and insulin resistance
- Primary source of vitamin D is sunlight
- Either Ergocalciferol or Cholecalciferol is recommended

Treatment with active vitamin D and calcium reduces bone loss after renal transplantation



Ruud G. L. de Sévaux et al. JASN 2002;13:1608-1614

- Dutch Study 111 renal transplant recipients (65 men, 46 women; were randomized to either treatment with active vitamin D (0.25 microg/d) plus calcium (1000 mg/d) (CaD group), or to no treatment (NoT group)

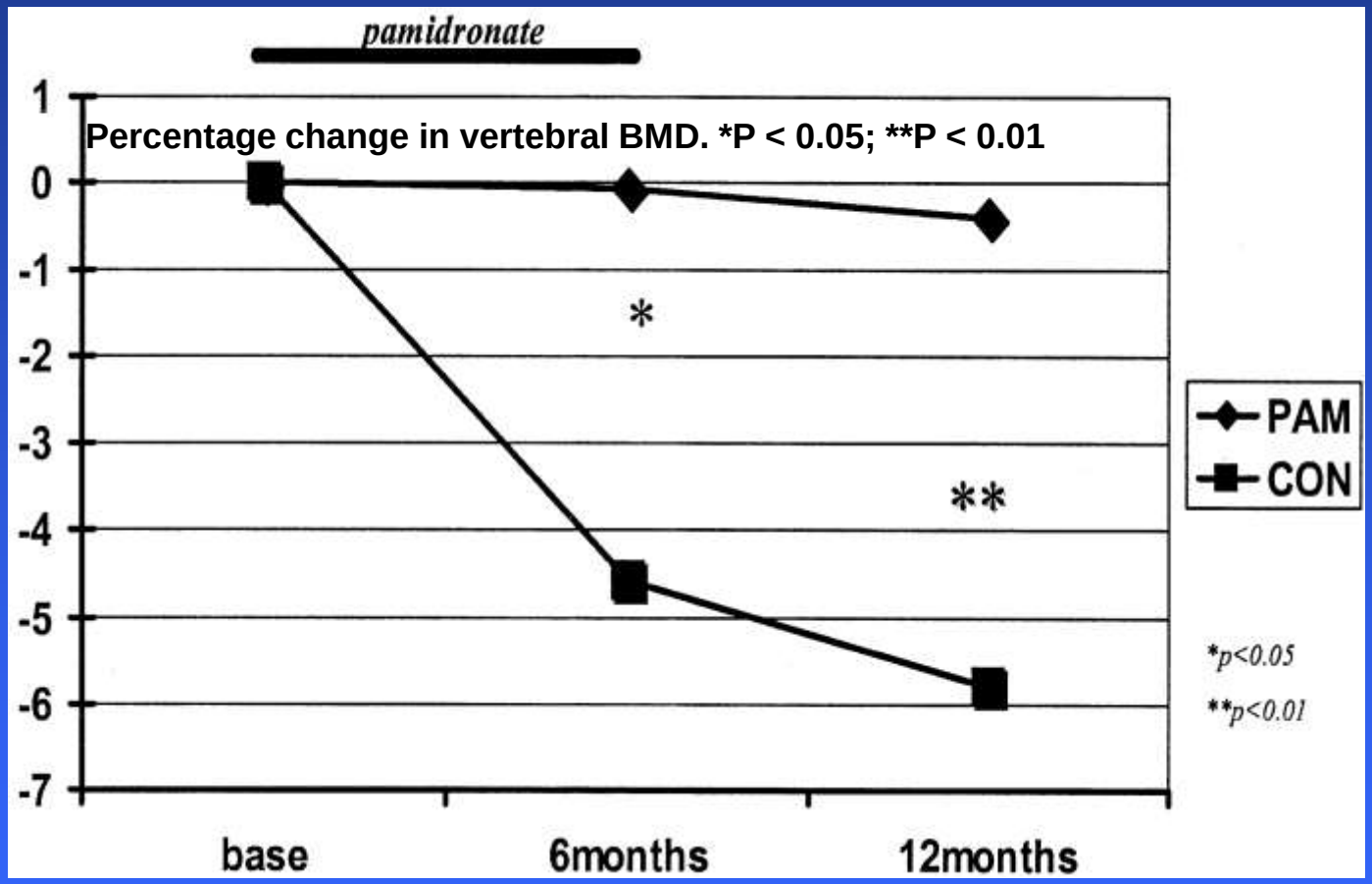
Active Vitamin D +/- calcium supplement

Oral active vitamin D with or without calcium supplement for at least 6 mo to 1 year after transplantation can also prevent early post-transplant bone loss and controlling hyperparathyroidism

Hypercalcemia and increased calcium load are major limiting factors

Since nutritional vitamin D supplement can provide the substrate (25-OH-D) for 1,25-OH2-D production, the decrease in PTH level was observed after cholecalciferol supplementation. However, the benefit of nutritional vitamin D in preservation of bone mass was inconsistent

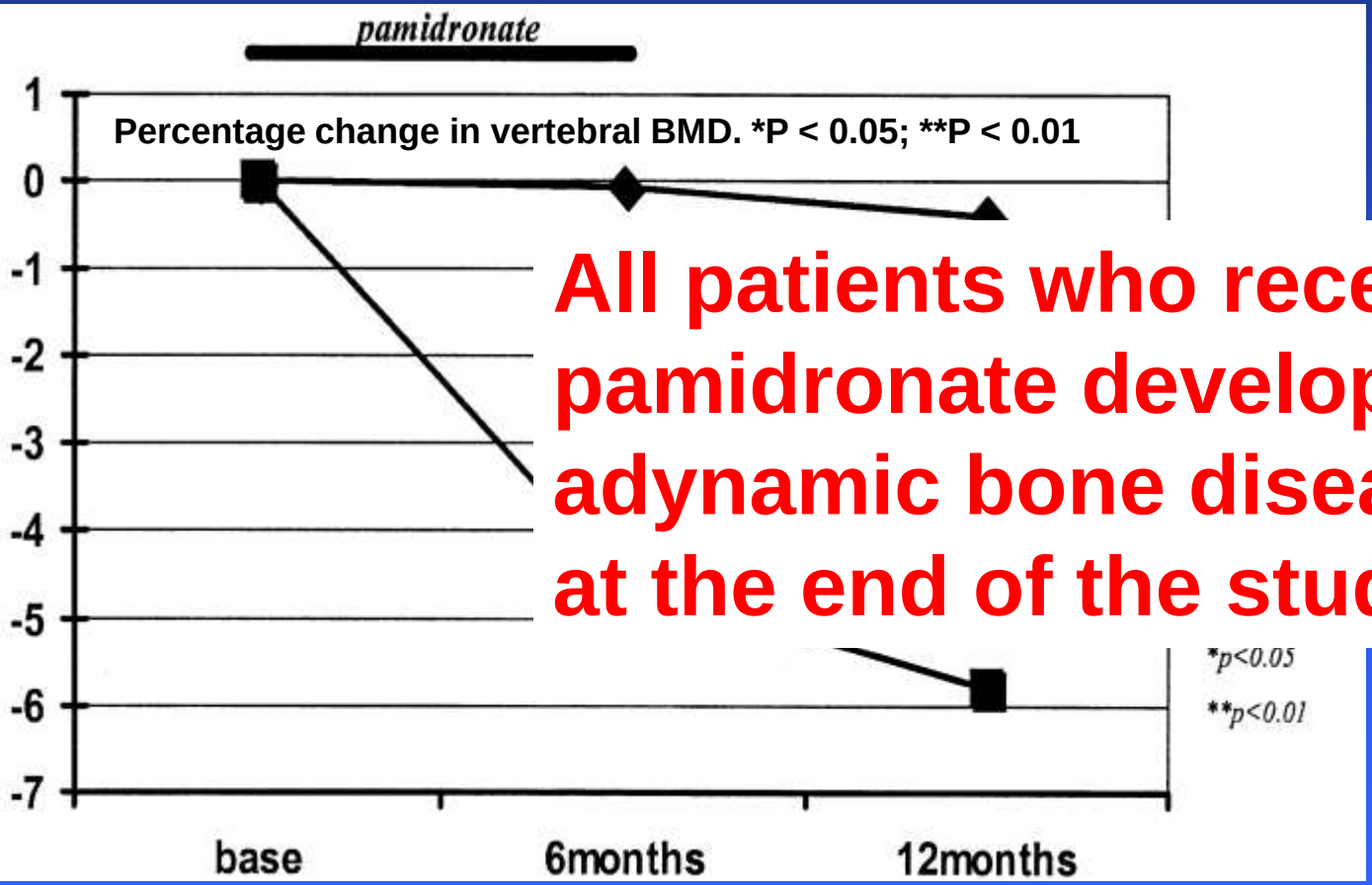
Prevention of bone loss in renal transplant recipients: a prospective, randomized trial of intravenous pamidronate



Maria Coco et al. JASN 2003;14:2669-2676

- US Study
- Pamidronate with vitamin D + Ca at baseline and at months 1, 2, 3, and 6 (n 31) Control subjects received vitamin D + Ca only Months 6 to 12, without pamidronate (n 28)
- Biochemical parameters of bone turnover were obtained monthly and BMD was obtained at baseline and months 6 and 12

Prevention of bone loss in renal transplant recipients: a prospective, randomized trial of intravenous pamidronate



All patients who received pamidronate developed adynamic bone disease at the end of the study

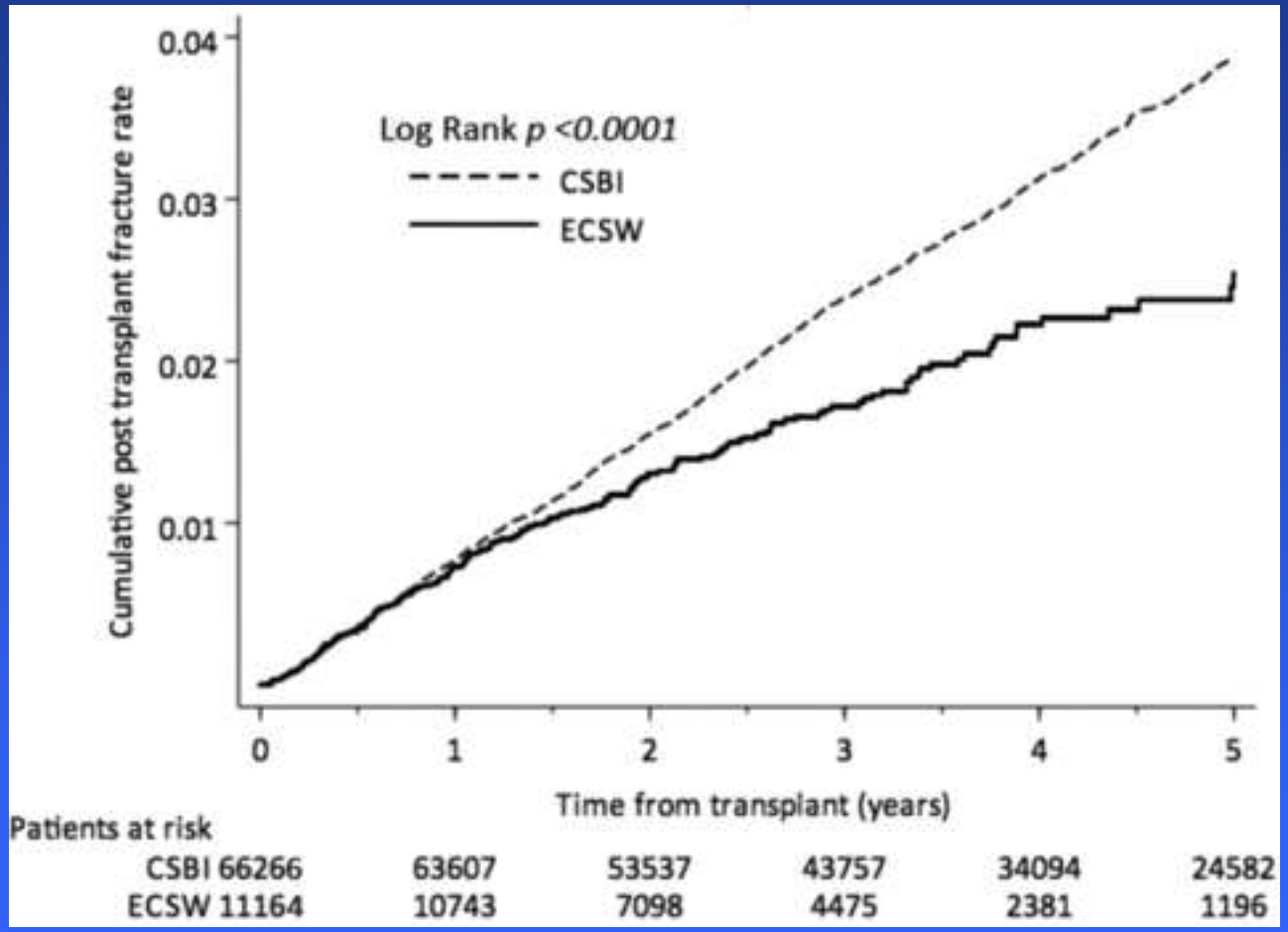
pamidronate with vitamin D + Ca at baseline and at months 1, 2, 3, and 6. Control subjects received D + Ca only. 6 to 12, without onate. Biochemical eters of bone r were obtained and BMD was obtained at baseline and months 6 and 12

Maria Coco et al. JASN 2003;14:2669-2676

Biphosphonates in CKD-MBD Post Transplant

- The systematic review of randomized controlled trials and the retrospective review of trials in prevention of early post-transplant bone loss revealed the superiority of a combined regimen of bisphosphonate and active vitamin D (± calcium) to active vitamin D (± calcium) alone in prevention of bone loss during the first year after transplantation but both regimens failed to show the favorable outcome in reducing fracture risk
- oral bisphosphonate with or without active vitamin D should be considered to KT recipients with osteopenia and/or osteoporosis during the first year after kidney transplantation. Nevertheless, care should be taken in giving bisphosphonate to patients with suspected adynamic bone disease. The benefit of bisphosphonate beyond the first 1-2 years remains unclear and will require further study

Steroid Withdrawal in CKD-MBD Post Transplant



Retrospective USRDS data. 77, 430 KT from 2000 to 2006. 1ry-Fracture incidence leading to hospitalization

CS withdrawal was associated with a 31% fracture risk reduction (HR 0.69; 95% CI 0.59-0.81).

Fractures associated with hospitalization are significantly lower with CS withdraw

American Journal of Transplantation
Volume 12, Issue 3, pages 649-659, 7 DEC 2011 DOI: 10.1111/j.1600-6143.2011.03872.x
http://onlinelibrary.wiley.com/doi/10.1111/j.1600-6143.2011.03872.x/full#f1

Calcimimetics

- Cinacalcet can used as an add-on therapy to active vitamin D in the treatment of secondary hyperparathyroidism in CKD
- Discontinuation of cinacalcet at the time of transplantation can cause rebound hypercalcemia and hyperparathyroidism resulting in an increase in the incidence of post-transplant nephrocalcinosis and parathyroidectomy

Cinacalcet for the treatment of hyperparathyroidism in kidney transplant recipients: a systematic review and meta-analysis.

Cohen JB[1], Gordon CE, Balk EM, Francis JM.

Author information

Abstract

BACKGROUND: Hyperparathyroidism is present in up to 50% of transplant recipients 1 year after transplant, often despite good graft function. Posttransplant patients frequently have hypercalcemia-associated hyperparathyroidism, limiting the role of vitamin D analogues and sometimes requiring parathyroidectomy. Multiple observational studies have investigated treatment of posttransplant hyperparathyroidism with the calcimimetic agent cinacalcet.

METHODS: We performed a systematic review and meta-analysis of prospective and retrospective studies from 2004 through January 26, 2012, using MEDLINE. We identified studies evaluating treatment with cinacalcet in renal transplant recipients with hyperparathyroidism. We performed random effects meta-analysis to determine changes in calcium, phosphorus, parathyroid hormone, and serum creatinine.

RESULTS: Twenty-one studies with 411 kidney transplant recipients treated with cinacalcet for hyperparathyroidism met inclusion criteria. Patients were treated for 3 to 24 months. By meta-analysis, calcium decreased by 1.14 mg/dL (95% confidence interval, -1.00 to -1.28), phosphorus increased by 0.46 mg/dL (95% confidence interval, 0.28-0.64), parathyroid hormone decreased by 102 pg/mL (95% confidence interval, -69 to -134), and there was no significant change in creatinine (0.02 mg/dL decrease; 95% confidence interval, -0.09 to 0.06). Cinacalcet resulted in hypocalcemia in seven patients. The most common side effect was gastrointestinal intolerance.

CONCLUSIONS: From nonrandomized studies, cinacalcet appears to be safe and effective for the treatment of posttransplant hyperparathyroidism. Larger observational studies and randomized controlled trials, performed over longer follow-up times and looking at clinical outcomes, are needed to corroborate these findings.

PMID: 23069843 [PubMed - indexed for MEDLINE]

Overall cinacalcet is a safe and effective therapy for hypercalcemia and persistent hyperparathyroidism after kidney transplantation and the effectiveness of cinacalcet is maintained for several years. There is no cut point as to how long the therapy should be continued since the severity and duration of hyperparathyroidism varies from patient to patient and, therefore, the time required for the shrinkage of enlarged hyperplastic parathyroid glands differs among patients

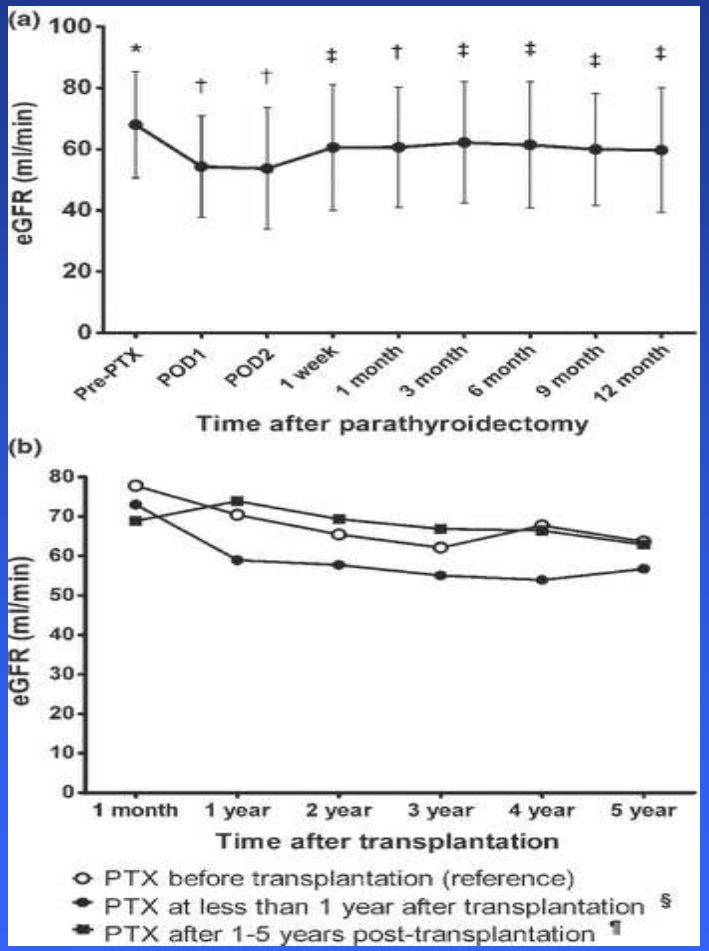
Parathyroidectomy Post Transplantation

- After parathyroidectomy, deterioration of allograft function is common with a 5%-30% drop in eGFR. The severity of baseline hyperparathyroidism seems to predict the decline in eGFR after surgery

- The cut-off values for PTH and serum calcium for PTX are not clear, PTX decision is mostly symptoms driven and varies between centers

- Subtotal to near total parathyroidectomy appears to result in a more favorable long-term outcome compared to total parathyroidectomy with auto transplantation

Impact of parathyroidectomy performed before and after kidney transplantation on allograft outcomes



- Korean Study -Retrospective, multi-center
- 63 patients who underwent PTX after kidney tx
- 37 patients who underwent PTX before transplantation
- eGFR values during the first 5 years after transplantation were significantly lower in the patients who underwent PTX less than 1 year after transplantation, than the pre transplant PTX patients

Volume 25, Issue 12, pages 1248-1256, 29 SEP 2012 DOI: 10.1111/j.1432-2277.2012.01564.x
http://onlinelibrary.wiley.com/doi/10.1111/j.1432-2277.2012.01564.x/full#f1

Conclusion

- CKD-MBD post transplant is prevalent and predispose to fractures, muscular, bone and joint pains, it is also associated with cardiovascular risk
- High dose corticosteroid and persistent hyperparathyroidism are the most important factors influencing CKD-MBD post transplant
- The use of active vitamin D with or without bisphosphonate may be useful in preventing early post-transplant bone loss
- Steroid withdrawal could be also beneficial in preservation of bone mass in long-term
- Calcimimetic is an alternative therapy to parathyroidectomy in KT recipients with persistent hyperparathyroidism

World J Transplant. 2015 Dec 24;5(4):231-42. doi: 10.5500/wjt.v5.i4.231.

Mineral and bone disorder after kidney transplantation.

Taweesedt PT[1], Disthabanchong S[1].

Author information

Abstract

After successful kidney transplantation, accumulated waste products and electrolytes are excreted and regulatory hormones return to normal levels. Despite the improvement in mineral metabolites and mineral regulating hormones after kidney transplantation, abnormal bone and mineral metabolism continues to present in most patients. During the first 3 mo, fibroblast growth factor-23 (FGF-23) and parathyroid hormone levels decrease rapidly in association with an increase in 1,25-dihydroxyvitamin D production. Renal phosphate excretion resumes and serum calcium, if elevated before, returns toward normal levels. FGF-23 excess during the first 3-12 mo results in exaggerated renal phosphate loss and hypophosphatemia occurs in some patients. After 1 year, FGF-23 and serum phosphate return to normal levels but persistent hyperparathyroidism remains in some patients. The progression of vascular calcification also attenuates. High dose corticosteroid and persistent hyperparathyroidism are the most important factors influencing abnormal bone and mineral metabolism in long-term kidney transplant (KT) recipients. Bone loss occurs at a highest rate during the first 6-12 mo after transplantation. Measurement of bone mineral density is recommended in patients with estimated glomerular filtration rate > 30 mL/min. The use of active vitamin D with or without bisphosphonate is effective in preventing early post-transplant bone loss. Steroid withdrawal regimen is also beneficial in preservation of bone mass in long-term. Calcimimetic is an alternative therapy to parathyroidectomy in KT recipients with persistent hyperparathyroidism. If parathyroidectomy is required, subtotal to near total parathyroidectomy is recommended. Performing parathyroidectomy during the waiting period prior to transplantation is also preferred in patients with severe hyperparathyroidism associated with hypercalcemia.

KEYWORDS: Bone mineral density; Phosphatonin; Phosphaturia; Renal transplantation; Tertiary hyperparathyroidism

PMID: 26722650 [PubMed] PMCID: PMC4689933 **Free PMC Article**


Thank you
Any Questions?

FGF-23 post transplant

- Recent research showed persistent post transplant elevations of fibroblast growth factor-23 (FGF-23) as playing a major role in post transplant hypophosphatemia and suppression of 1α-hydroxylase activity in the kidney
- Although FGF-23 levels are reported to decline rapidly after transplant, there is limited information regarding its relationship to mineral metabolism in prevalent kidney transplant recipients

Abstract ▾ Send to: ▾

See 1 citation found using an alternative search:

Am J Nephrol. 2008;28(2):246-53. Epub 2007 Nov 7.

Abnormal bone and mineral metabolism in kidney transplant patients--a review.

Sprague SM[1], Belozeroff V, Danese MD, Martin LP, Olgaard K.

Author information

Abstract

BACKGROUND/AIMS: Abnormal bone and mineral metabolism is common in patients with kidney failure and often persists after successful kidney transplant.

METHODS: To better understand the natural history of this disease in transplant patients, we reviewed the literature by searching MEDLINE for English language articles published between January 1990 and October 2006 that contained Medical Subject Headings and key words related to secondary or persistent hyperparathyroidism and kidney transplant.

RESULTS: Parathyroid hormone levels decreased significantly during the first 3 months after transplant but typically stabilized at elevated values after 1 year. Calcium tended to increase after transplant and then stabilize at the higher end of the normal range within 2 months. Phosphorus decreased rapidly to within or below normal levels after surgery and hypophosphatemia, if present, resolved within 2 months. Low levels of 1,25(OH)2 vitamin D typically did not reach normal values until almost 18 months after transplant.

CONCLUSION: This review provides evidence demonstrating that abnormal bone and mineral metabolism exists in patients after kidney transplant and suggests the need for treatment of this condition. However, better observational and interventional research is needed before advocating such a treatment guideline.

PMID: 17989497 [PubMed - indexed for MEDLINE] Free full text

Publication Types, MeSH Terms, Substances

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Review 1alpha(OH)D3 On cholecalciferol--an active vit

Review Mineral metabolism patients with chronic kidr [E

[Changes in bone and mine kidney transplant patients w

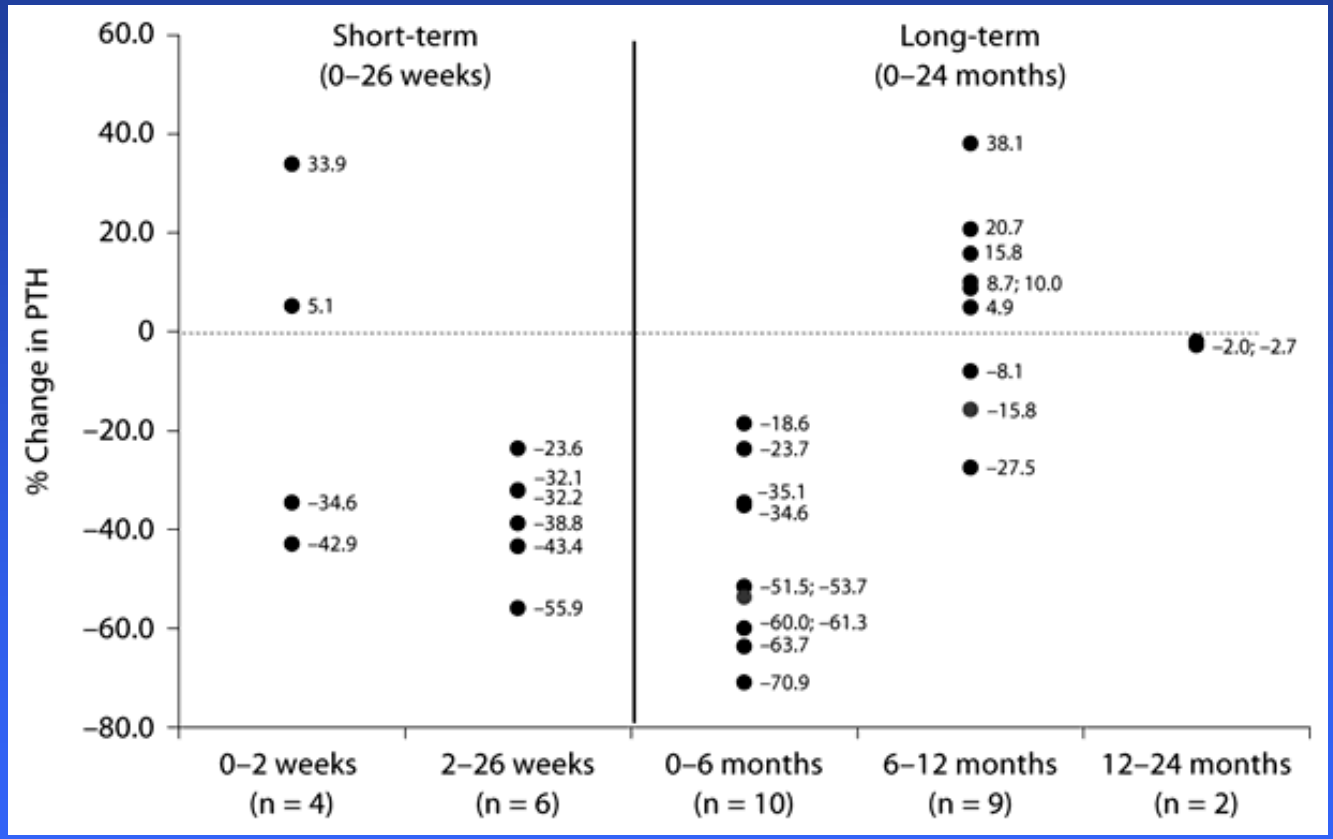
Bone mineral metabolism a kidney disease in [Nephrol

Cited by 6 PubMed Cent

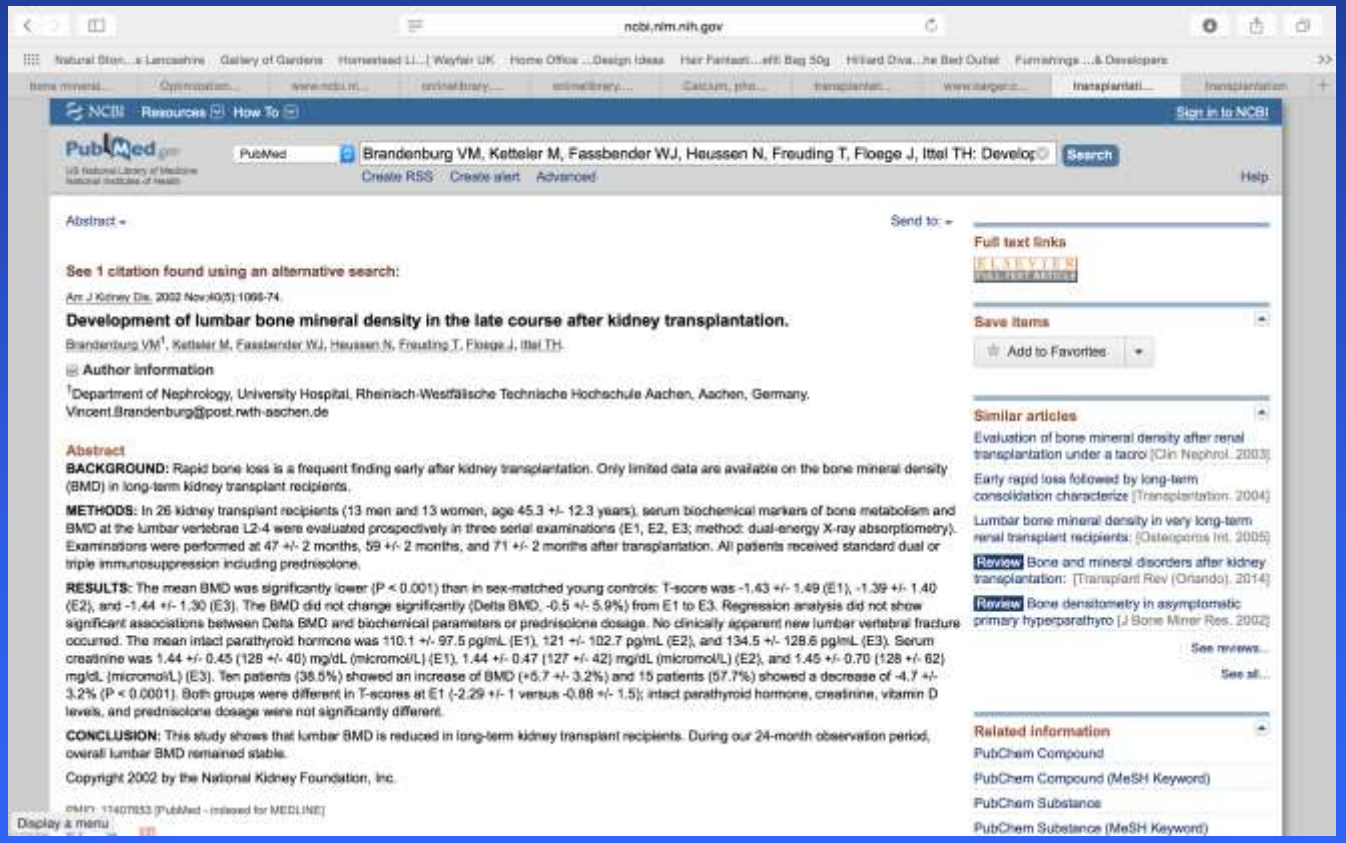
Serum osteoprotegerin is as pressure in kidney transplan

A Prospective Cohort Study Metabolism After Kidney T [

- 557 articles - 424 articles were eliminated and 133 submitted for full article review
- 38 publications reporting data on the natural progression of HPT in kidney transplant patients and associated outcomes were accepted
- Analyses were based on data from 2,486 patients enrolled in 38 studies


Short-term
(0–26 weeks)
Long-term
(0–24 months)
% Change in PTH
60.0
40.0
20.0
0
–20.0
–40.0
–60.0
–80.0
33.9
5.1
–34.6
–42.9
–23.6
–32.1
–32.2
–38.8
–43.4
–55.9
–18.6
–23.7
–35.1
–34.6
–51.5; –53.7
–60.0; –61.3
–63.7
–70.9
38.1
20.7
15.8
8.7; 10.0
4.9
–8.1
–15.8
–27.5
–2.0; –2.7
0–2 weeks
(n = 4)
2–26 weeks
(n = 6)
0–6 months
(n = 10)
6–12 months
(n = 9)
12–24 months
(n = 2)

HPT, which develops during chronic kidney failure, often persists after kidney transplantation. While elevated PTH and Ca levels associated with this disorder have been associated with adverse effects on various outcomes in dialysis patients, observational and interventional studies are limited in transplant patients, especially with respect to clinical outcomes. Treating HPT in kidney transplant patients may have the potential of improving patient outcomes, but more research is needed in these patients to better assess long-term treatment benefits on clinical outcomes.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Development of lumbar bone mineral density in the late course after kidney transplantation.
Brandenburg VM[1], Ketteler M, Fassbender WJ, Heussen N, Freuding T, Floege J, Ittel TH.
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Abstract
BACKGROUND: Rapid bone loss is a frequent finding early after kidney transplantation. Only limited data are available on the bone mineral density (BMD) in long-term kidney transplant recipients.
METHODS: In 26 kidney transplant recipients (13 men and 13 women, age 45.3 +/- 12.3 years), serum biochemical markers of bone metabolism and BMD at the lumbar vertebrae L2-4 were evaluated prospectively in three serial examinations (E1, E2, E3; method: dual-energy X-ray absorptiometry). Examinations were performed at 47 +/- 2 months, 59 +/- 2 months, and 71 +/- 2 months after transplantation. All patients received standard dual or triple immunosuppression including prednisolone.
RESULTS: The mean BMD was significantly lower (P < 0.001) than in sex-matched young controls: T-score was -1.43 +/- 1.49 (E1), -1.39 +/- 1.40 (E2), and -1.44 +/- 1.30 (E3). The BMD did not change significantly (Delta BMD, -0.5 +/- 5.9%) from E1 to E3. Regression analysis did not show significant associations between Delta BMD and biochemical parameters or prednisolone dosage. No clinically apparent new lumbar vertebral fracture occurred. The mean intact parathyroid hormone was 110.1 +/- 97.5 pg/mL (E1), 121 +/- 102.7 pg/mL (E2), and 134.5 +/- 128.6 pg/mL (E3). Serum creatinine was 1.44 +/- 0.45 (128 +/- 40) mg/dL (micromol/L) (E1), 1.44 +/- 0.47 (127 +/- 42) mg/dL (micromol/L) (E2), and 1.45 +/- 0.70 (128 +/- 62) mg/dL (micromol/L) (E3). Ten patients (38.5%) showed an increase of BMD (+5.7 +/- 3.2%) and 15 patients (57.7%) showed a decrease of -4.7 +/- 3.2% (P < 0.0001). Both groups were different in T-scores at E1 (-2.29 +/- 1 versus -0.88 +/- 1.5); intact parathyroid hormone, creatinine, vitamin D levels, and prednisolone dosage were not significantly different.
CONCLUSION: This study shows that lumbar BMD is reduced in long-term kidney transplant recipients. During our 24-month observation period, overall lumbar BMD remained stable.
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Elevated PTH levels were associated with loss of bone in kidney transplant patients. Low BMD (T score !–2.5), however, was frequently diagnosed in kidney transplant patients and has been associated with significant morbid- ity in these patients

Transplantation. 2013 Aug 15;96(3):290-6. doi: 10.1097/TP.0b013e3182985468.

Persistence of bone and mineral disorders 2 years after successful kidney transplantation.

Neves CL[1], dos Reis LM, Batista DG, Custodio MR, Graciolli FG, Martin Rde C, Neves KR, Dominguez WV, Moyses RM, Jorgetti V.

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Abstract

BACKGROUND: Studies that have conducted bone biopsies after kidney transplantation are scarce, and the results are conflicting.

METHODS: We evaluate the bone histomorphometry, in vitro proliferation, and alkaline phosphatase expression in osteoblasts isolated from bone biopsies from 27 kidney transplant patients. The patients had preserved renal function and were treated with the same immunosuppressive therapy, receiving a minimum dose of corticosteroids.

RESULTS: The biochemical analysis revealed that 41% of the patients presented with hypercalcemia, 26% presented with hypophosphatemia, and hypovitaminosis D was detected in 63%. The histomorphometric analysis showed a reduced trabecular number and increased trabecular separation, mineral apposition rate, and mineralization lag time, as well as higher osteoid surface, osteoblastic surface, resorption surface, and osteoclastic surface and a lower mineralizing surface, compared with the controls. Based on the TMV classification, bone turnover was normal in 48%, high in 26%, and low in 26% of patients. Bone mineralization was delayed in 48% of the patients, and 58% of the patients with hypovitaminosis D presented with delayed bone mineralization. Bone volume was low in 37% of the patients. The osteoblasts from patients exhibited a higher degree of proliferation compared with those from controls.

CONCLUSION: Eight-two percent of our patients presented with alterations in at least one of the TMV parameters. Persistence of hyperparathyroidism, hypovitaminosis D, and immunosuppressive drugs may have influenced osteoblast function, which would explain many of the bone alterations found in these patients.

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